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Molecular Docking Analysis of PVDF Membrane Against Human Erα, EGFR, CDK2, mTOR, and HSP90 Proteins

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Abstract

Porous membranes are used in biological and chemical systems and industrial applications. Polyvinylidene fluoride film (PVDF) membrane is a commercial membrane used in drug delivery, protein immobilization, food industry, tissue engineering, and medical devices. Because of providing a large surface area in this study PVDF membrane is used.
Molecular docking is a molecular modeling simulation software especially used to determine protein-ligand interactions. The aim of the study is to determine the interaction of hydrophobic PVDF membranes on Erα, EGFR, CDK2, mTOR, and HSP90 proteins by docking method and to examine its potential as a possible drug carrier. The three-dimensional structure of the receptors has been acquired from the RCSB protein data bank and is docked with 3D PubChem of PVDF using AutoDock 1.5.6 software. The results have shown that the PVDF membrane had the best docking score for mTOR between the investigated proteins.

Keywords: PVDF membrane, mTOR, drug carrier, molecular docking

1. Introduction

Drugs could be adsorbed to the surface of carriers and can be used as drug delivery systems in applications as gene therapy, protein delivery, radiotherapy, and vaccine delivery [1]. Polymeric micelles, liposomes, xanthan gum, alginate, dendrimers (PAMAM, PPI, peptide), inorganic nanoparticles, nanocrystals, and quantum dots are examples of biopolymeric materials. Additionally, polymers, cell-membranes, peptides, and antibodies are examples of nanocarriers in drug release [2].
Membranes have a key role in transport efficiency and the transport factors depend on the type of liquids used as a membrane phase. Because of porous structures that provide a surface area for organic phases, ionic liquids, enzymes, specific complexing agents [3], and protein immobilization [4-7]. Polyvinylidene fluoride film (PVDF) membrane is a synthetic membrane used in various applications such as to separate contaminating viral particles from biologically important proteins [8], metal extraction [9], drug delivery [10], pharmaceuticals removal [11], amino acid immobilization [12] and protein immobilization [4-7]. Baican et al., Akashi and Kuroda, Schmidt et.al studied protein bovine serum albumin immobilization into different pore sizes of PVDF

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[4,5,7]. Vasile et al. expressed that plasma treated PVDF is a good substrate for protein coating, and they immobilized triglycine and protein A on a PVDF surface. [13]. Pâslaru et al., immobilized Immunoglobulin G on the PVDF surface [6].
Several receptors are linked to cancer control like estrogen receptor (Erα), epidermal growth factor receptor (EGFR), Cyclin-dependent kinase 2 (CDK2), mammalian target of rapamycin (mTOR), and heat shock protein 90 (HSP90) [16]. So much so that treatment to be discovered on these proteins shows promise for cancer treatment.
In this present work, we aimed to obtain the interaction of PVDF membranes on Erα, EGFR, CDK2, mTOR, and HSP90 proteins by using AutoDock 1.5.6 software.

2. Materials and Method

The molecular docking approach is used to model the interaction between a molecule and a protein at the atomic level. This situation allows us to characterize the behavior of molecules in the binding site of target proteins and elucidate fundamental biochemical processes [15].
In this study, the interaction between the hydrophobic PVDF molecule and Erα, EGFR, CDK2, mTOR, and HSP90 proteins have been evaluated by molecular docking. In this context, our work has progressed in three mechanisms:

a) Preparation of Protein: The crystal structure of Erα (PDB ID: 2IOK), EGFR (PDB ID: 2J6M), CDK2 (PDB ID: 4RJ3), mTOR (PDB ID: 4DRH), and HSP90 (PDB ID: 2VCJ) proteins were retrieved from the RCSB Protein Data Bank [16].

b) Preparation of Ligand: The 3D molecular structure of the PVDF molecule (PubChem CID: 6369) was retrieved from chemical databases PubChem Data Bank [17].

c) Docking Calculation and Visualization: Polar hydrogens opened with the programmed protein AutoDock (ADT) program were added and distributed throughout the structure by adding the Kollman loads. For the ligand, torsion roots and torsion numbers were determined with ADT. Subsequently, AD4 atomic types were identified as required by the AutoDock and Vina Docking input files for ligand and protein constructs. Grid parameters including protein and ligand were determined. Windows command prompt was opened, the input file path was opened, and Vina command parameters were entered. The calculation process started, and the final result was evaluated.

3. Results

The docking results calculated by the Vina for Erα (ligand 1), EGFR (ligand 1), CDK2 (ligand 1), mTOR (ligand 1), and HSP90 (ligand 1) proteins were -3.3 kcal/mol, -2.7 kcal/mol, -3.0 kcal/mol, -3.3 kcal/mol, and -2.8 kcal/mol respectively [Table 1]. Results displayed that the hydrophobic PVDF molecule showed a high affinity towards mTOR and Erα proteins [19].

Table 1. Protein-Ligand Molecular Docking Results

Protein ID	Ligand ID	Binding affinity (kcal/mol)
2IOK	6369	-3.3
2J6M	6369	-2.7
4RJ3	6369	-3.0
4DRH	6369	-3.3
2VCJ	6369	-2.8

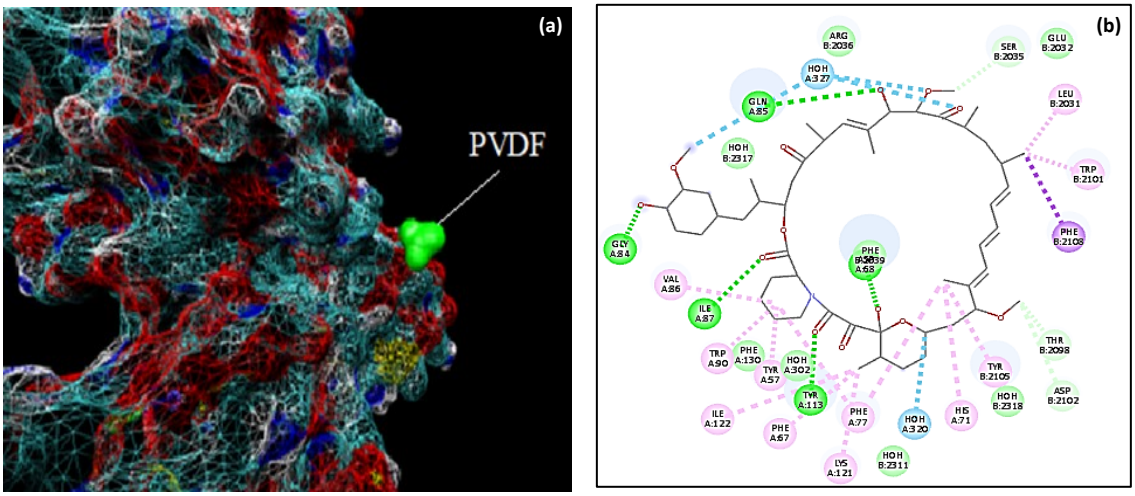

Figure 1. 3D ligand interaction diagram of PVDF with mTOR protein.

The AutoDock Vina result of PVDF with mTOR protein is visualized in Figure 1(a). In the image, the PVDF (shown in green color) molecule forms a tight compact with the human mTOR protein. Undoubtedly, the BioDiscovery results shown in Figure 1(b) also support this interaction. Hydrogen bond interactions between the PVDF membrane and mTOR are established by amino acids such as glycine, isoleucine, and tyrosine in the mTOR protein. This binding energy is reported in Table 1 as -3.3 kcal/mol.

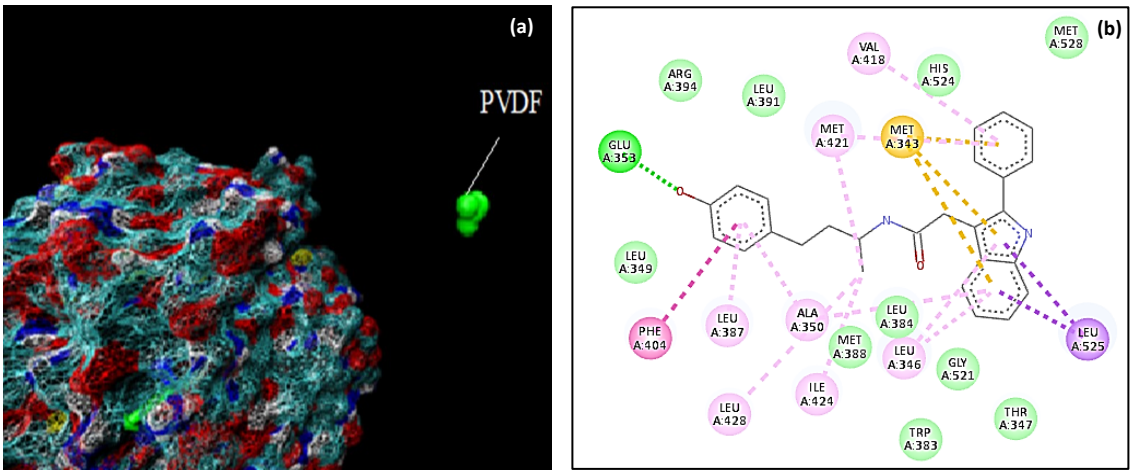

Figure 2. 3D ligand interaction diagram of PVDF with Erα protein.

The AutoDock Vina result PVDF with Erα protein is visualized in Figure 2 (a). In the image, the human Erα protein and the PVDF (shown in green color) molecule showed a less compact structure compared to the mTOR protein. The hydrogen bond interaction between the PVDF membrane and Erα was established with the amino acid glutamate. This binding energy is reported in Table 1 as -3.3 kcal/mol.

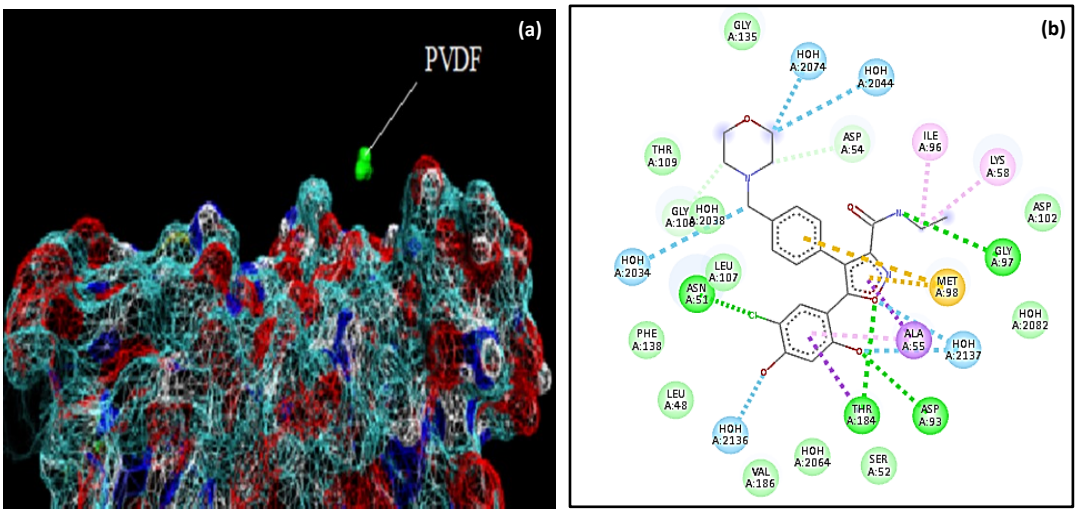

Figure 3. 3D ligand interaction diagram of PVDF with HSP90 protein.

The AutoDock Vina result of PVDF with HSP90 protein is visualized in Figure 3 (a). In the image, the human HSP90 protein and the PVDF (shown in green color) molecule showed a less compact structure compared to the mTOR protein. The hydrogen bond interaction between the PVDF membrane and HSP90 was established with the amino acid tyrosine, glycine, and asparagine. This binding energy is reported in Table 1 as -2.8 kcal/mol.

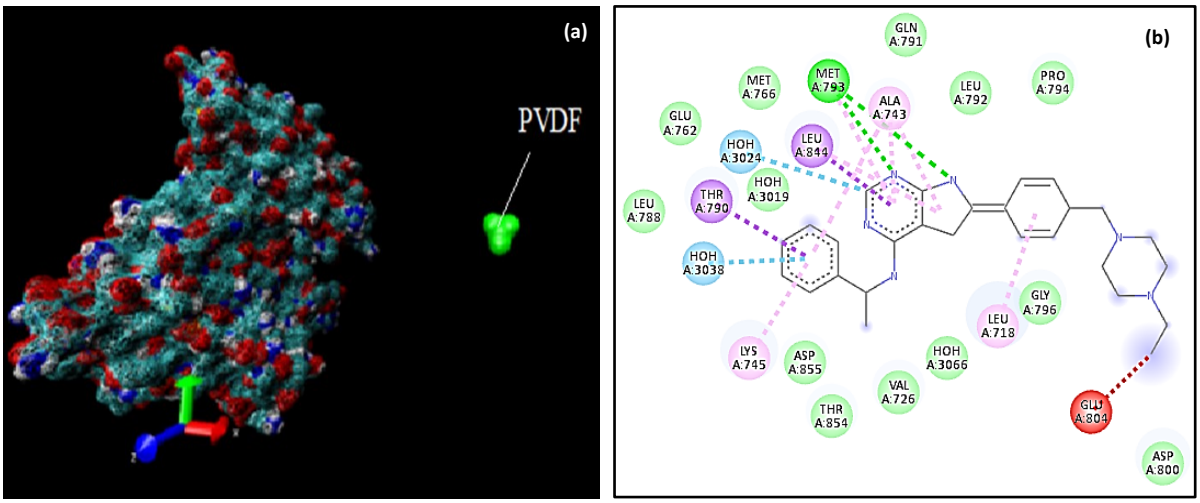

Figure 4. 3D ligand interaction diagram of PVDF with EGFR protein.

The AutoDock Vina result of PVDF with EGFR protein is visualized in Figure 4 (a). In the image, the human EGFR protein and the PVDF (shown in green color) molecule showed the least interaction compared to other proteins. Undoubtedly, the BioDiscovery results shown in Figure 4 (b) also support this interaction. The hydrogen bond interaction between the PVDF membrane and EGFR was established with methionine amino acid. This binding energy is reported in Table 1 as -2.7 kcal/mol.

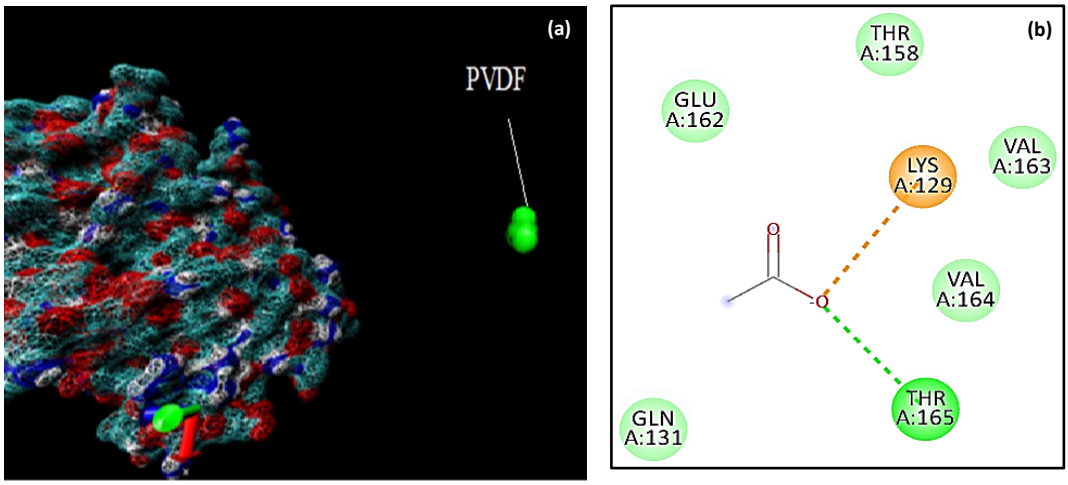

Figure 5. 3D ligand interaction diagram of PVDF with CDK2 protein.

The AutoDock Vina result of PVDF with CDK2 protein is visualized in Figure 5 (a). In the image, the human CDK2 protein and the PVDF (shown in green color) molecule showed a less compact structure compared to the mTOR protein. The hydrogen bond interaction between the PVDF membrane and CDK2 was established with tyrosine amino acid. This binding energy is reported in Table 1 as -3.0 kcal/mol.

4. Discussion and Conclusion

Targeted drug therapy has gained significant momentum in recent years, as of its non-specific effects drug therapy. Especially, liposomes, micelles, dendrimers, and monoclonal antibodies are nanomaterials used for targeted drug therapy. These structures use active and passive targeting strategies to deliver the active substance to the targeted cells. The use of active targeting increases transport to cellular levels and selective transport of the pharmacological agent to the site of action is ensured. However, studies have also reported that these nanostructures cause undesirable effects in cells such as apoptosis, necrosis, autophagy, and mitotic destruction. So, can a new alternative nanocarrier overcome these side effects? Undoubtedly, nanoscientists have sought the answer to this question. Akashi and Kuroda tested the PVDF membrane as a new nanocarrier in 2014 [5]. In the study, they expressed that the interaction of the hydrophobic PVDF membrane with the protein is substantial. Because of its porous structure and the obtained interaction between the studied proteins of this present work, the usability of the PVDF membrane could be tested in further experimental work but it is needed to clarify the exact molecular mechanism underlying this study. Additionally, Schmidt et al. mentioned the use of a modified PVDF membrane by radiation-induced graft immobilization method can be possible to immobilize proteins [7]. This could be an alternative tested factor to enhance the immobilization yield of protein.
In light of these studies, we analyzed the interaction of the PVDF membrane with the human protein. In the study, PVDF-Erα, PVDF-EGFR, PVDF-CDK2, PVDF-mTOR, and PVDF-HSP90 interactions are reported. Comparably a human-serum protein/ membrane interaction with a modified PVDF membrane with zwitterionic is studied in the literature [18]. By the binding affinities of Erα, EGFR, CDK2, mTOR, and HSP90 receptors our study showed that the PVDF compound could be a potential ligand by docking method. Thus, it can be used as a PVDF molecule, a novel, and natural drug carrier molecule. However, in vitro and in vivo research are required to support these consequences.

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